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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,808	10/16/2003	Steven K. Burke	1932.2135-002	8791

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EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,808	BURKE, STEVEN K.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9 and 12-42* is/are rejected.

7)☒ Claim(s) *6-8,10, and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 – 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treatment of a mammal with a risk factor for bone loss, does not reasonably provide enablement for the method of prophylaxis, or prevention, of bone loss in a mammal with a risk factor for bone loss. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 104 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex part Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the relative skill of those in the art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

1. The nature of the invention and the state of the prior art

The claimed invention relates to the prevention of bone loss in a mammal that has a risk factor for bone loss, which encompasses both any mammal and any risk factor for bone loss. There are many potential risk factors for bone loss, such as age, gender, diet, lifestyle, postmenopause, drug side effects, etc. While the state of the art is relatively high with regard to the treatment of bone loss with specific agents, it is underdeveloped with regard to the generic prevention of bone loss.

2. The predictability of the art, the relative skill of those in the art, and the quantity of experimentation necessary

Given the great diversity between the potential risk factors for bone loss, there is a factor of unpredictability with regard to the prevention of bone loss. Thus, a considerable amount of empirical testing is required with no *a prior* expectation of success by one of ordinary skill in the art before prevention of bone loss resulting from one risk factor, for example, age, would also prevent bone loss resulting from another risk factor, for example, smoking or drug use.

3. The breadth of the claims, the amount of direction or guidance provided and the presence or absence of working examples

The claims are very broad and inclusive of "prophylactic treatment of a mammal at risk factor for bone loss" by administration of at least one amine polymer. The

specification provides no direction or example for ascertaining the effectiveness of the *prevention* of bone loss, though it is noted that examples for the assessment of the effectiveness of *treatment* of bone density loss in hemodialysis patients was disclosed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15 – 19, 31, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumagai *et al.* (US 5,837,674).

Kumagai *et al.* disclose a method for the treatment or prevention of conditions associated with bone loss or weakness using polypeptides. The polypeptides are representative of amine-containing polymers, especially when amino acid side chains such as arginine and/or lysine are chosen for R_1 (column 6 or claim 2). The polypeptides can be aliphatic by the selection appropriate amino acid side chains for R_1 and R_2 (column 6). The amount of polymer that is administered is from 0.1% to 99.9% of a formulation (column 10, lines 16 – 18). Dosage amounts range from 100 μg/kg to

20 mg/kg per single dosage (column 11, lines 1 – 10), and are within the scope of the instantly claimed therapeutic amount of polymer, depending on the size of the patient. The polymers are useful for the treatment of any condition associated with bone loss or weakness (column 7, lines 8 – 12). Subjects who benefit from administration of the polylpeptides are those who, *for any reason*, have bone loss or weakening (column 11, lines 14 – 16). Moreover, postmenopausal osteoporosis is specifically recognized as a risk factor for bone loss (column 1, lines 62 – 65). Osteoporosis is a particular condition that is especially amenable to treatment with the polypeptides taught by Kumagai *et al.* (column 11, lines 17 – 18).

Claims 15, 19 – 29, and 31 – 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes-Farley *et al.* (US 5,667,775).

Holmes-Farley *et al.* disclose a method for removing phosphate from a patient by ion exchange comprising orally administering a therapeutically effective amount of a composition comprising an aliphatic amine polymer (sevelamer) characterized by a repeat unit having the formula shown in claim 1. The polymer backbone can be polyallylamine, polyvinylamine or poly(aminoethyl)acrylate (column 2, lines 38 – 49). The variable regions of the polymer meet the claimed structural limitations, as R is representative of hydrogen, an unsubstituted alkyl, and/or a substituted alkyl. The substituents can also be selected from quaternary ammonium or other functional groups (see claims 1, 5, 14, and 19). The polymer is crosslinked with a crosslinking agent, such as epichlorohydrin, which is present in the composition from about 0.5 to about

75% by weight (see claim 2). Holmes-Farley *et al.* teach that sevelamer provides an effective treatment for decreasing serum phosphate levels by binding phosphate in the gastrointestinal tract, without concomitantly increasing the absorption of any clinically undesirable materials, particularly calcium or aluminum (column 2, lines 10 – 15). The polymers are useful for the treatment of hyperphosphatemia (abstract). Because patients suffering from hyperphosphatemia can be considered to be at risk for bone loss, the administration of sevelamer to such patients is a method for treatment of a mammal that has a risk factor for bone loss.

The method of Holmes-Farley includes the same step of administering the same polymer as that of the instantly claimed method. Because it is known in the art that patients suffering from hyperphosphatemia are at risk for the development of osteoporosis, the step performed by Holmes-Farley to remove phosphate from an individual for the treatment of hyperphosphatemia would inherently treat osteoporosis as well. It is noted that claims 33 – 42 could be favorably considered if claim 31 were amended such that the specific polymers of claim 33 were administered, rather than a generic amine polymer, and also to include the negative proviso of claim 1 whereby the mammal is not suffering from hyperphosphatemia or the phrase "to a patient in need thereof."

Claims 1, 14, 15, 30, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Young *et al.* (US 2003/0224501, which benefits from provisional application US 60/356749 filed 2/15/02).

Young *et al.* disclose BMP polypeptides useful for inducing cartilage and bone formation. The polypeptides are representative of amine-containing polymers, due to the presence of amine-containing amino acid side chains such as arginine (i.e. SEQ. ID 30). The polypeptides can be administered immediately prior to, during, or immediately after nutrient consumption (e.g., a meal) (see paragraph 0999). The polypeptides may be used in the diagnosis, prognosis, prevention, and/or treatment of diseases and/or disorders associated with aberrant bone formation and/or cell proliferation and differentiation (paragraph 0459). The polypeptides may also be used in the diagnosis, prognosis, prevention, and/or treatment of musculoskeletal diseases and disorders, bone growth disorders, and osteoporosis, which is known to be a disease with a risk factor for bone loss (paragraph 0466).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 5, 9, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trollsas *et al.* (6,458,889).

Trollsas *et al.* teach polyfunctional hydrophilic polymers and methods for their use, which include tissue augmentation (i.e. growth, formation, etc.). The polymers may contain amine groups, may be aliphatic, and specifically may be polyvinylamines (column 7, line 4), which are within the scope of several figures of instant claim 4, especially the first two figures of page 24 when $R_1 = R_2 = H$. The polymer may be a homopolymer (column 5, line 67). The polymers are crosslinked with a crosslinking agent (abstract). An effective amount of the polymer is a "tissue growth-promoting amount," which is defined as the amount needed to stimulate tissue growth to a detectable degree. The specific tissue may include bone tissue (column 8, lines 13 – 22). Because the crosslinked polymers, which may include polyvinylamines, taught by Trollas et al. promote tissue growth, which may include bone tissue, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize an amine polymer as a method of promoting bone formation to patients in need thereof with a reasonable expectation of success.

Claim Objections

Claims 6 – 8, 10, and 11 are objected to as being dependent upon a rejected

base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER